

In the Specification

**Please replace the paragraph found on page 19, lines 14-24 of the specification with the following paragraph:**

The functionally-equivalent polypeptides of the first aspect of the invention may also be polypeptides which have been identified using one or more techniques of structural alignment. For example, the ~~Inpharmatica Genome Threader~~<sup>TM</sup> INPHARMATICA GENOME THREADER technology that forms one aspect of the search tools used to generate the Biopendium search database may be used (see co-pending International Patent Application No. PCT/GB01/01105) to identify polypeptides of presently-unknown function which, while having low sequence identity as compared to the INSP097 polypeptide, are predicted to be alpha-2 macroglobulin-like proteinases, said method utilising a polypeptide of the first aspect of the invention, by virtue of sharing significant structural homology with the INSP097 polypeptide sequences. By "significant structural homology" is meant that the ~~Inpharmatica Genome Threader~~<sup>TM</sup> INPHARMATICA GENOME THREADER predicts two proteins to share structural homology with a certainty of at 10% and above.

**Please replace the paragraph found on page 28, lines 2-22 of the specification with the following paragraph:**

In many cases, isolated cDNA sequences will be incomplete, in that the region encoding the polypeptide will be cut short, normally at the 5' end. Several methods are available to obtain full length cDNAs, or to extend short cDNAs. Such sequences may be extended utilising a partial nucleotide sequence and employing various methods known in the art to detect upstream sequences such as promoters and regulatory elements. For example, one method which may be employed is based on the method of Rapid Amplification of cDNA Ends (RACE; see, for example, Frohman *et al.*, PNAS USA 85, 8998-9002, 1988). Recent modifications of this technique, exemplified by the ~~Marathon~~<sup>TM</sup> MARATHON technology (Clontech Laboratories Inc.), for example, have significantly simplified the search for longer cDNAs. A slightly different technique, termed "restriction-site" PCR, uses universal primers to retrieve unknown nucleic acid sequence adjacent a known locus (Sarkar, G. (1993) PCR Methods Applic. 2:318-322). Inverse PCR may also be used to amplify or to

extend sequences using divergent primers based on a known region (Triglia, T. *et al.* (1988) *Nucleic Acids Res.* 16:8186). Another method which may be used is capture PCR which involves PCR amplification of DNA fragments adjacent a known sequence in human and yeast artificial chromosome DNA (Lagerstrom, M. *et al.* (1991) *PCR Methods Applic.*, 1, 111-119). Another method which may be used to retrieve unknown sequences is that of Parker, J.D. *et al.* (1991); *Nucleic Acids Res.* 19:3055-3060). Additionally, one may use PCR, nested primers, and ~~PromoterFinder~~<sup>TM</sup> PROMOTERFINDER libraries to walk genomic DNA (Clontech, Palo Alto, CA). This process avoids the need to screen libraries and is useful in finding intron/exon junctions.

**Please replace the paragraph found on page 31, line 20 through page 32, line 8 of the specification with the following paragraph:**

In addition to control sequences, it may be desirable to add regulatory sequences that allow for regulation of the expression of the polypeptide relative to the growth of the host cell. Examples of regulatory sequences are those which cause the expression of a gene to be increased or decreased in response to a chemical or physical stimulus, including the presence of a regulatory compound or to various temperature or metabolic conditions. Regulatory sequences are those non-translated regions of the vector, such as enhancers, promoters and 5' and 3' untranslated regions. These interact with host cellular proteins to carry out transcription and translation. Such regulatory sequences may vary in their strength and ~~speeifeity~~specificity. Depending on the vector system and host utilised, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the Bluescript phagemid (Stratagene, LaJolla, CA) or ~~pSport~~<sup>TM</sup> PSPORTL plasmid (Gibco BRL) and the like may be used. The baculovirus polyhedrin promoter may be used in insect cells. Promoters or enhancers derived from the genomes of plant cells (for example, heat shock, RUBISCO and storage protein genes) or from plant viruses (for example, viral promoters or leader sequences) may be cloned into the vector. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are preferable. If it is necessary to generate a cell line that contains multiple copies of the sequence, vectors based on SV40 or EBV may be used with an appropriate selectable marker.

**Please replace the paragraph found on page 45, lines 20-21 of the specification with the following paragraph:**

The technology referred to as jet injection (see, for example, [www.powderjet.com](http://www.powderjet.com)) may also be useful in the formulation of vaccine compositions.

**Please replace the paragraph found on page 53, lines 5-17 of the specification with the following paragraph:**

Gene-specific cloning primers INSP097-CP1 and INSP097-CP2 (Figures 3 & 4 and Table 1) were designed to amplify a cDNA fragment of 412 bp spanning the receptor binding domain of the INSP097 prediction. The primer pair was used with a range of  $\lambda$  cDNA library samples as templates. The PCR was performed in a final volume of 50  $\mu$ l containing 1X-AmpliTaq<sup>TM</sup> AMPLITAQ buffer, 200  $\mu$ M dNTPs, 50 pmoles each of cloning primer, 2.5 units of-AmpliTaq<sup>TM</sup> AMPLITAQ (Perkin Elmer) and 100 ng of each  $\lambda$  cDNA library template using an MJ Research DNA Engine, programmed as follows: 94°C, 2 min; 40 cycles of 94°C, 1 min, 55°C, 1 min, and 72°C, 1 min; followed by 1 cycle at 72°C for 7 min and a holding cycle at 4°C. The amplification products were visualized on 0.8 % agarose gels in 1 X TAE buffer (Invitrogen). PCR products migrating at the predicted molecular mass were purified from the gel using the Wizard PCR Preps DNA Purification System (Promega). The PCR product was eluted in 50  $\mu$ l of sterile water and either subcloned directly or stored at -20°C.